

09/763,740

=> d his

(FILE 'HOME' ENTERED AT 12:46:36 ON 01 MAY 2002)

FILE 'REGISTRY' ENTERED AT 12:47:08 ON 01 MAY 2002
L1 STRUCTURE UPLOADED
L2 1 S L1
L3 22 S L1 FUL

FILE 'REGISTRY' ENTERED AT 12:48:04 ON 01 MAY 2002
L4 1 S L3

FILE 'CAPLUS' ENTERED AT 12:48:15 ON 01 MAY 2002
L5 1 S L3

FILE 'REGISTRY' ENTERED AT 12:50:01 ON 01 MAY 2002

FILE 'REGISTRY' ENTERED AT 12:50:58 ON 01 MAY 2002
L6 STRUCTURE UPLOADED
L7 19 S L6 FUL

FILE 'CAPLUS' ENTERED AT 12:51:22 ON 01 MAY 2002
L8 2 S L7

=> d l6

L6 HAS NO ANSWERS

L6 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> d bib abs hitstr 1-2

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 2001:662560 CAPLUS
DN 135:352345
TI Statistical Molecular Design, Parallel Synthesis, and Biological
Evaluation of a Library of Thrombin Inhibitors
AU Linusson, Anna; Gottfries, Johan; Olsson, Thomas; Oernskov, Eivor;
Folestad, Staffan; Norden, Bo; Wold, Svante
CS AstraZeneca R&D Molndal, Moelndal, S-431 83, Swed.
SO Journal of Medicinal Chemistry (2001), 44(21), 3424-3439
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB A library of thrombin inhibitors has been designed using statistical mol.
design. An arom. scaffold was used, with three varied positions
corresponding to three pockets at the active site of thrombin (the S-, P-,
and D-pockets). The selection was performed in the building block space,
and previously acquired data were included in the design procedure. The
design resulted in six, four, and six building blocks for the first (S),
second (P), and third (D) pockets, resp. A second round of selection
applied to the combined selected building blocks resulted in a subset of
18 compds. The selected library was synthesized in parallel and biol.
evaluated. The compds. were analyzed with respect to their inhibition
(pIC50) of thrombin; membrane permeability, estd. by migration behavior in
micellar media (CE log k') and pKa; and specificity with respect to
inhibition (Ki) of trypsin. Multivariate QSAR studies of the responses
yielded valuable results and information that could only be found using
statistical mol. design in combination with multivariate anal.

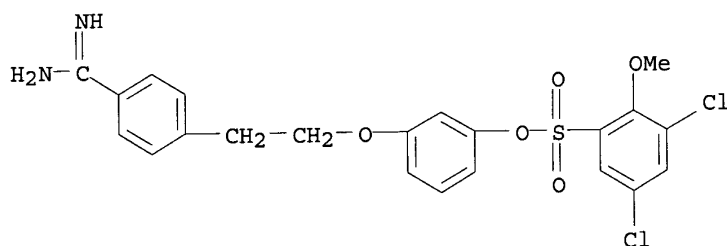
09/763,740

IT 372523-37-0P 372523-38-1P 372523-39-2P
372523-40-5P 372523-41-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(statistical mol. design, parallel synthesis, and biol. evaluation of a library of thrombin inhibitors)

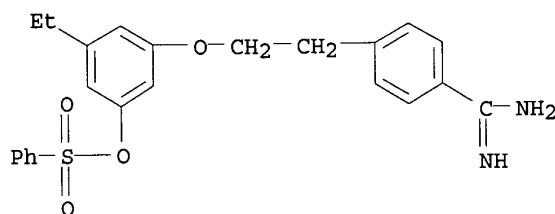
RN 372523-37-0 CAPLUS

CN Benzenesulfonic acid, 3,5-dichloro-2-methoxy-, 3-[2-[4-(aminoiminomethyl)phenyl]ethoxy]phenyl ester (9CI) (CA INDEX NAME)



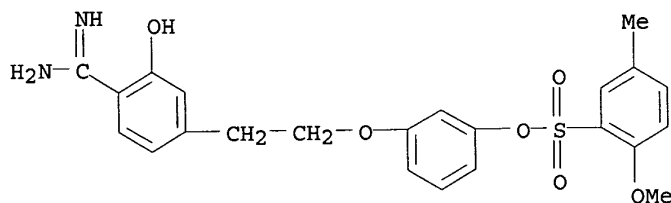
RN 372523-38-1 CAPLUS

CN Benzenecarboximidamide, 4-[2-[3-ethyl-5-[(phenylsulfonyl)oxy]phenoxy]ethyl]- (9CI) (CA INDEX NAME)



RN 372523-39-2 CAPLUS

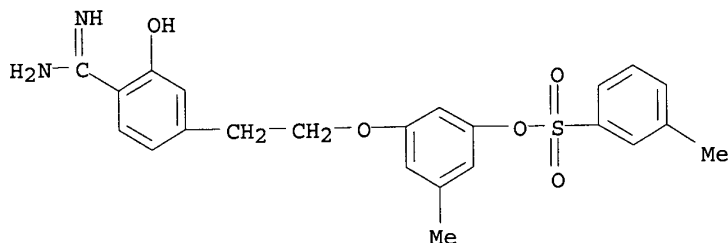
CN Benzenesulfonic acid, 2-methoxy-5-methyl-, 3-[2-[4-(aminoiminomethyl)-3-hydroxyphenyl]ethoxy]phenyl ester (9CI) (CA INDEX NAME)



RN 372523-40-5 CAPLUS

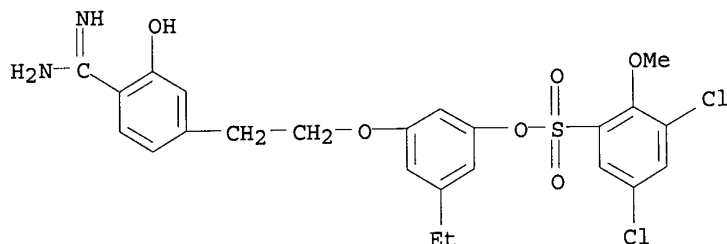
CN Benzenesulfonic acid, 3-methyl-, 3-[2-[4-(aminoiminomethyl)-3-hydroxyphenyl]ethoxy]-5-methylphenyl ester (9CI) (CA INDEX NAME)

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RN 372523-41-6 CAPLUS

CN Benzenesulfonic acid, 3,5-dichloro-2-methoxy-, 3-[2-[4-(aminoiminomethyl)-3-hydroxyphenyl]ethoxy]-5-ethylphenyl ester (9CI) (CA INDEX NAME)



RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS

AN 1998:65889 CAPLUS

DN 128:127826

TI Preparation of new amidino derivatives as thrombin inhibitors

IN Antonsson, Thomas

PA Astra Aktiebolag, Swed.; Antonsson, Thomas

SO PCT Int. Appl., 108 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|------------|--|----------|-----------------|----------|
| PI | WO 9801422 | A1 | 19980115 | WO 1997-SE1150 | 19970626 |
| | W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| | CA 2260190 | AA | 19980115 | CA 1997-2260190 | 19970626 |
| | AU 9735628 | A1 | 19980202 | AU 1997-35628 | 19970626 |
| | AU 726236 | B2 | 20001102 | | |
| | EP 917528 | A1 | 19990526 | EP 1997-932085 | 19970626 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |
| | BR 9710142 | A | 19990810 | BR 1997-10142 | 19970626 |
| | CN 1228765 | A | 19990915 | CN 1997-197578 | 19970626 |

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| | | | | |
|----------------------|----|----------|----------------|----------|
| JP 2000515505 | T2 | 20001121 | JP 1998-505123 | 19970626 |
| US 6221898 | B1 | 20010424 | US 1997-894833 | 19970829 |
| NO 9806180 | A | 19990304 | NO 1998-6180 | 19981229 |
| KR 2000022437 | A | 20000425 | KR 1998-710870 | 19981230 |
| US 2002040043 | A1 | 20020404 | US 2001-839609 | 20010423 |
| PRAI SE 1996-2646 | A | 19960704 | | |
| WO 1997-SE1150 | W | 19970626 | | |
| US 1997-894833 | A3 | 19970829 | | |
| OS MARPAT 128:127826 | | | | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

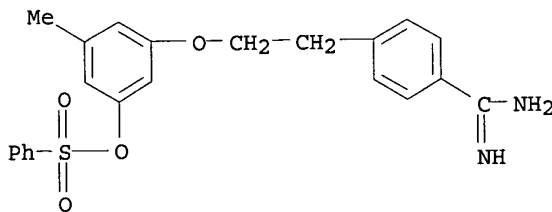
AB The title compds. [I; one of R1 and R2 = Z-SO₂-Ar1 and the other = R4; Z = O, NR5; R3 = Oh, halo, Cn, etc.; R4 = H, OH, halo, etc.; Ar1 = Ph, C1-3 alkylphenyl, naphthyl, etc.; R5 = H, C1-6 alkyl, Ph, C1-3 alkylphenyl; Y = O, S, S(O), SS(O)₂, NR22; R22 = H, C1-4 alkyl; n = 0-4; B = II, III, IV, V; X1, X2 = a single bond, CH₂], useful as competitive inhibitors of trypsin-like proteases, such as thrombin, and in particular in the treatment of conditions where inhibition of thrombin is required (e.g. thrombosis) or as anticoagulants, were prepd. Thus, reaction of 3-[2-(4-cyanophenyl)ethoxy]aniline with benzenesulfonyl chloride followed by treatment of the resulting N-{3-[2-(4-cyanophenyl)ethoxy]phenyl}benzene sulfonamide with HCl(g) in EtOH, and treating N-{3-[2-(4-ethoxyiminomethylphenyl)ethoxy]phenyl}benzenesulfonamide.HCl with NH₃(g) afforded the title compd. VI. The title compds. I described herein were tested for thrombin inhibition and were found to exhibit an IC₅₀ and/or K_i (as appropriate) of < 0.3 .mu.M.

IT 201933-66-6P 201934-29-4P 201934-30-7P
201934-31-8P 201934-32-9P 201934-33-0P
201934-34-1P 201934-35-2P 201934-36-3P
201934-37-4P 201934-77-2P 201935-45-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of new amidino derivs. as thrombin inhibitors)

RN 201933-66-6 CAPLUS

CN Benzenecarboximidamide, 4-[2-[3-methyl-5-[(phenylsulfonyl)oxy]phenoxy]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

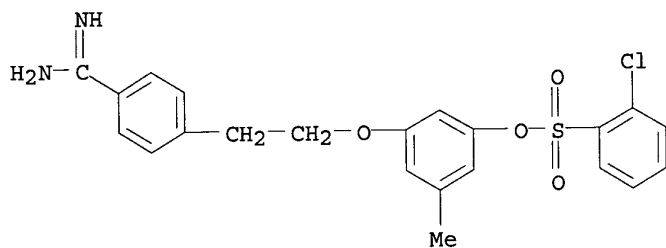


● HCl

RN 201934-29-4 CAPLUS

CN Benzenesulfonic acid, 2-chloro-, 3-[2-[4-(aminoiminomethyl)phenyl]ethoxy]-5-methylphenyl ester (9CI) (CA INDEX NAME)

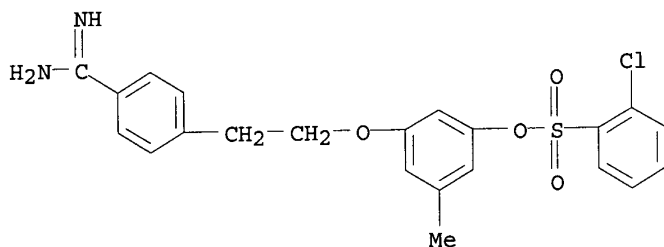
09/763,740



RN 201934-30-7 CAPLUS
CN Benzenesulfonic acid, 2-chloro-, 3-[2-[4-(aminoiminomethyl)phenyl]ethoxy]-5-methylphenyl ester, monoacetate (9CI) (CA INDEX NAME)

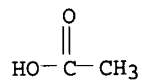
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CRN 201934-29-4
CMF C22 H21 Cl N2 O4 S

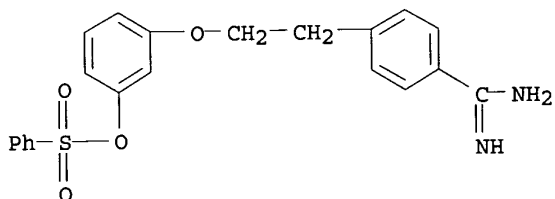


CM 2

CRN 64-19-7
CMF C2 H4 O2



RN 201934-31-8 CAPLUS
CN Benzenecarboximidamide, 4-[2-[3-[(phenylsulfonyl)oxy]phenoxy]ethyl]- (9CI)
(CA INDEX NAME)

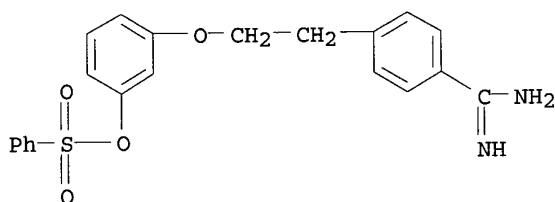


09/763,740

RN 201934-32-9 CAPLUS
CN Benzenecarboximidamide, 4-[2-[3-[(phenylsulfonyl)oxy]phenoxy]ethyl]-, monoacetate (9CI) (CA INDEX NAME)

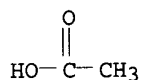
CM 1

CRN 201934-31-8
CMF C21 H20 N2 O4 S

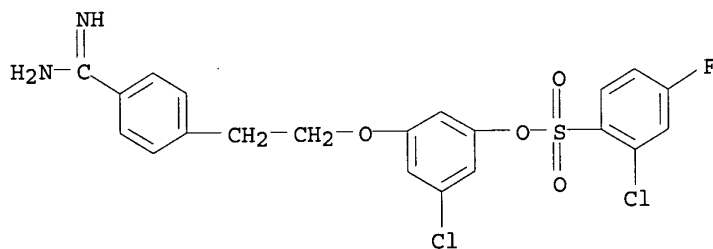


CM 2

CRN 64-19-7
CMF C2 H4 O2



RN 201934-33-0 CAPLUS
CN Benzenesulfonic acid, 2-chloro-4-fluoro-, 3-[2-[4-(aminoiminomethyl)phenyl]ethoxy]-5-chlorophenyl ester (9CI) (CA INDEX NAME)

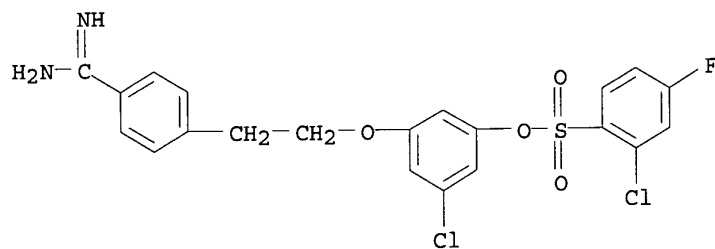


RN 201934-34-1 CAPLUS
CN Benzenesulfonic acid, 2-chloro-4-fluoro-, 3-[2-[4-(aminoiminomethyl)phenyl]ethoxy]-5-chlorophenyl ester, monoacetate (9CI) (CA INDEX NAME)

CM 1

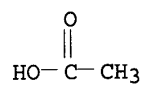
CRN 201934-33-0
CMF C21 H17 Cl2 F N2 O4 S

09/763,740

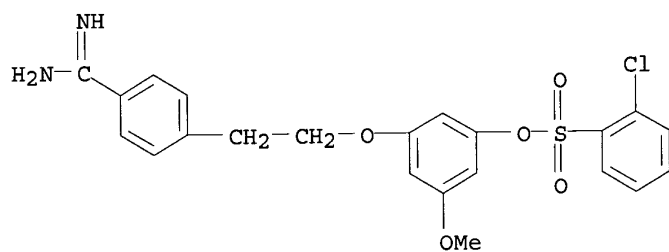


CM 2

CRN 64-19-7
CMF C2 H4 O2

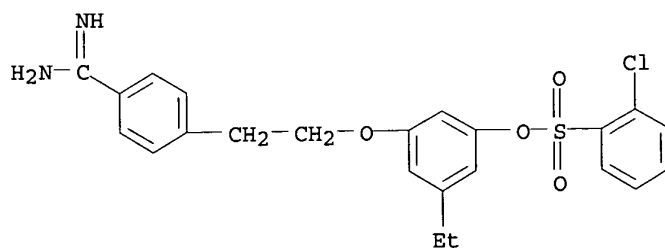


RN 201934-35-2 CAPLUS
CN Benzenesulfonic acid, 2-chloro-, 3-[2-[4-(aminoiminomethyl)phenyl]ethoxy]-5-methoxyphenyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 201934-36-3 CAPLUS
CN Benzenesulfonic acid, 2-chloro-, 3-[2-[4-(aminoiminomethyl)phenyl]ethoxy]-5-ethylphenyl ester (9CI) (CA INDEX NAME)



09/763,740

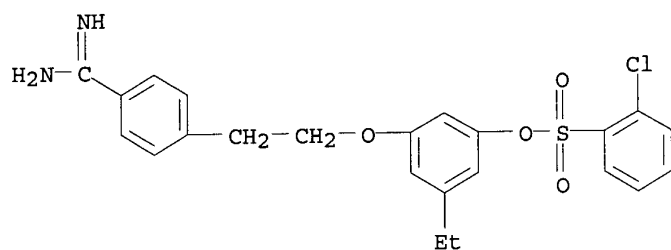
RN 201934-37-4 CAPLUS

CN Benzenesulfonic acid, 2-chloro-, 3-[2-[4-(aminoiminomethyl)phenyl]ethoxy]-5-ethylphenyl ester, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 201934-36-3

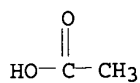
CMF C23 H23 Cl N2 O4 S



CM 2

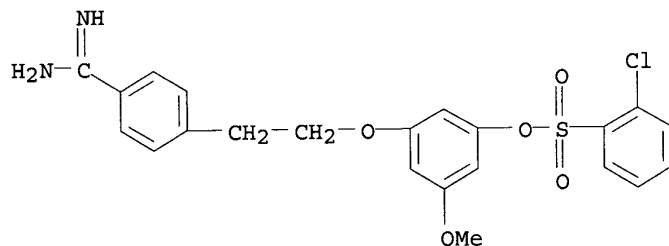
CRN 64-19-7

CMF C2 H4 O2



RN 201934-77-2 CAPLUS

CN Benzenesulfonic acid, 2-chloro-, 3-[2-[4-(aminoiminomethyl)phenyl]ethoxy]-5-methoxyphenyl ester (9CI) (CA INDEX NAME)



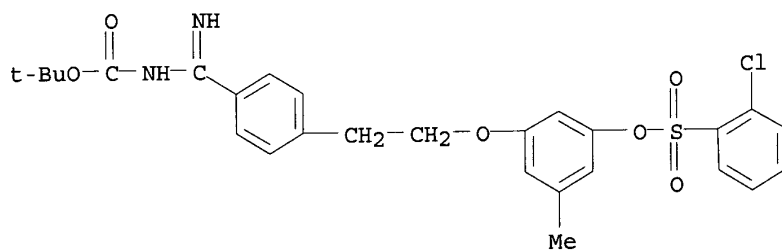
RN 201935-45-7 CAPLUS

CN Benzenecarboximidamide, 4-[2-[3-methyl-5-[(phenylsulfonyl)oxy]phenoxy]ethyl]- (9CI) (CA INDEX NAME)

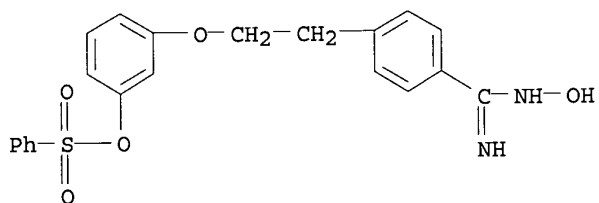
Cc1ccc(OCCc2ccc(C(=N)N)cc2)cc1OS(=O)(=O)c3ccccc3

201935-29-7P 201935-31-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of new amidino derivs. as thrombin inhibitors)

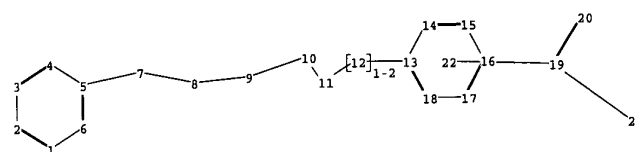
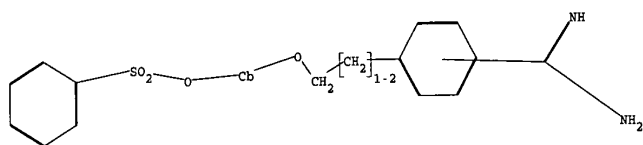
RN 201935-29-7 CAPLOS
 CN Benzenesulfonic acid, 2-chloro-, 3-[2-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]iminomethyl]phenyl]ethoxy]-5-methylphenyl ester (9CI) (CA INDEX NAME)



RN 201935-31-1 CAPLUS
CN Benzenecarboximidamide, N-hydroxy-4-[2-[3-[(phenylsulfonyl)oxy]phenoxy]eth
yl]- (9CI) (CA INDEX NAME)

 \Rightarrow

C:\STNEXP4\QUERIES\839.str



chain nodes :

7 8 9 10 11 12 19 20 21

ring nodes :

1 2 3 4 5 6 13 14 15 16 17 18

chain bonds :

5-7 7-8 8-9 9-10 10-11 11-12 12-13 19-20 19-21

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 13-14 13-18 14-15 15-16 16-17 17-18

exact/norm bonds :

7-8 19-20 19-21

exact bonds :

5-7 8-9 9-10 10-11 11-12 12-13

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 13-14 13-18 14-15 15-16 16-17 17-18

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS

Generic attributes :

9:

Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System : Monocyclic

Element Count :

Node 9: Limited
C,C6